"A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHORUS POISONING"

Dissertation submitted in partial fulfillment of the

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHORUS POISONING"** submitted by **Dr.K.SIVASANKAR** to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment for the award of Doctor of Medicine is a bonafide work carried out by him under my guidance and supervision during the academic year 2009-2012. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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DECLARATION

I, Dr.K.SIVASANKAR, solemnly declare that the dissertation titled **"A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHORUS POISONING"** has been prepared by me.

This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MD Degree Branch I (General Medicine).

It was not submitted to the award of any degree/diploma to any University either in part or in full previously

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Date: Dr.K.SIVASANKAR

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CONTENTS

INTRODUCTION

Self inflicted violence accounts for almost half of the 1.6 million violent deaths that occur every year worldwide. About 63% of global deaths from self harm occur in the Asia Pacific region. According to National Crime Records Bureau India, every 5 minutes a person commits suicide and 7 attempt to kill themselves, forming about 1,00,000 deaths per year.[1] Suicide rate was highest in the state of Kerala.[2] Majority of the victims belonged to the age group 14- 34 Years[3] and Organo Phosphorus Compounds (OPC) were the most common agent used for suicide purpose.[4]

With the advance of times, pesticides are now a days widely used for modern cultivation methods. Hence, they are readily available as over the counter drugs even in village shops and act as common agents for suicidal purposes. Currently pesticide self poisoning has become a major clinical problem of the developing countries [5,6] killing around 3,00,000 people each year[7,8].Most of these deaths occur in rural areas, where easy access to highly toxic pesticides turns many impulsive acts of self poisoning into suicide.[9]

In India OPC intake is the commonest method of suicide (40.5%) after hanging (49%). Hospital-based data suggest that barbiturates and copper sulfate were the commonly used agents for suicide in the years, 1972-1977; however, later they were replaced by OP compounds and aluminium phosphide. Organo phosphorus insecticides are responsible for as much as 75% of all poisonings in our country today.[10]

The gastrointestinal symptoms following Organophosphorus compound poisoning are excessive salivation, nausea, vomiting, abdominal pain and diarrhea. Both in experimental studies[11,12] and in humans exposed to these compounds pancreatic damage has been reported. Pancreatic injury in humans may be painless [13] and marked by hyperamylasemia, elevated serum lipase, hyperglycemia and glycosuria. Occasionally, symptomatic acute pancreatitis can occur.[14] The incidence of the latter varies from 7–22% depending on type of study and compound.[15] The present study was undertaken to find the incidence of hyperamylasemia in OPC poisoning and to identify the relation between hyperamylasemia and acetylcholinesterase (AChE) levels, which is widely used as an indicator of clinical severity

REVIEW OF LITERATURE

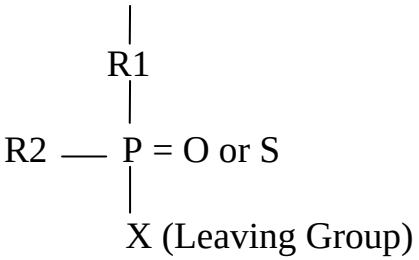
ORGANOPHOSPHATES – A BACKGROUND

History

The first potent synthetic organic phosphorus anticholinesterase was Tetraethylpyrophosphate (TEPP), which was synthesized by Clermont in 1854. [16] In 1932, Lange and Krueger wrote of choking and blurred vision following inhalation of dimethyl and diethyl phosphorofluoridates. This account inspired Schrader in Germany to begin investigating these agents, initially as pesticides, and later for use in warfare. During this research, Schrader's group synthesized hundreds of compounds, including the popular pesticide Parathion and the chemical warfare agents Sarin, Soman, and Tabun. Allied scientists were also motivated during the same period by the work, and independently discovered other extremely toxic compounds such as Diisopropylphosphofluoridate (DFP).[17] Since that time, it is estimated that more than 50,000 organic phosphorus compounds have been synthesized and screened for pesticidal activity, with dozens being produced commercially.

BASIC STRUCTURE

Organophosphorus compounds are basically esters of phosphoric acid or of phosphorothioic acids [18]. The basic formula is:



The R (R1, R2) denotes either aromatic or aliphatic (ethyl or methyl) group. The X is called the leaving group and is the principal metabolite for species identification .It determines many of the characteristics of the compound and provides a means of classifying OPC's into 4 main groups.[19] The Organothiophosphates which contain double bonded sulphur group are converted into organophosphates in the liver.

Group 1 compounds contain quarternary nitrogen at the X position, and are collectively termed Phosphorylcholines. These chemicals originally developed as weapons of war[20] are powerful cholinesterase inhibitors and can also directly stimulate cholinergic receptors, presumably because of their structural resemblance to Acetyl choline(Ach).

Group 2 compounds are called Fluorophosphates because they possess a fluorine molecule as the leaving group. Like group 1 compounds, these compounds are volatile and highly toxic, making them well-suited for chemical warfare.

Group 3 compounds contain a cyanide molecule or a halogen other than fluorine. The most well-known agents in this group are Cyanophosphates such as Tabun.

The fourth group is the broadest and comprises various subgroups based on the configuration of the R_1 and R_2 groups, with the majority falling into the category of either a dimethoxy or diethoxy compound. Most of the insecticides in use today fall into this last class.[20]

PHARMACOLOGY

The onset and severity of OP poisoning is determined by the degree, route of exposure, the lipid solubility and rate of metabolism of the particular compound and activation in liver, required before the compound is active.

OP compounds and carbamates are generally highly lipid soluble and hence may be systemically absorbed and can cause toxic effects within minutes after exposure. They are well absorbed by inhalation, ocular exposure, across any mucosal surface, the skin and throughout the gastrointestinal tract (GIT). Skin exposure is extremely important, as many cases of toxicity occur after cutaneous exposure alone. Exposure by inhalation results in the fastest appearance of toxic symptoms, followed by the gastrointestinal route and finally the dermal route.

Direct acting OP agents function to inhibit cholinesterase directly, and do not require bio-activation in the liver. The insecticide Dichlorvos is an example of a direct inhibitor[4.] Indirect inhibitors require oxidation by the gastrointestinal mucosa and liver to active forms, which then inhibit ChE. Most of the commonly encountered insecticides such as Malathion and Parathion are indirect agents and require bio-activation before manifesting toxicity. Most of the indirect inhibitors undergo desulfuration in the intestinal mucosa and liver following absorption to form the more active phosphate metabolites.[21]

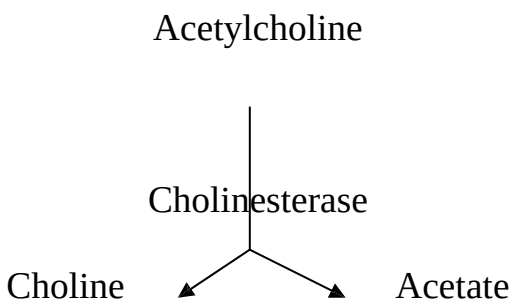
The practical importance of this classification is that direct inhibitors cause symptoms and signs quickly during or after exposure, whereas in the case

of indirect inhibitors symptoms and signs appear later and the effects last longer after cessation of exposure.

Because OP agents are more fat soluble, they may accumulate in the body's fat stores which act as a *"reservoir"*, prolonging elimination and toxic effects. This has been reported for more lipophilic compounds such as Fenthion and Chlorfenthion.

PATHOPHYSIOLOGY OF OPC POISONING

The primary mechanism of action of OP pesticides is inhibition of acetylcholinesterase (AChE), which is an enzyme found in the nervous system. Its normal action is to breakdown acetylcholine (ACh) into acetate and choline. Choline is reused.



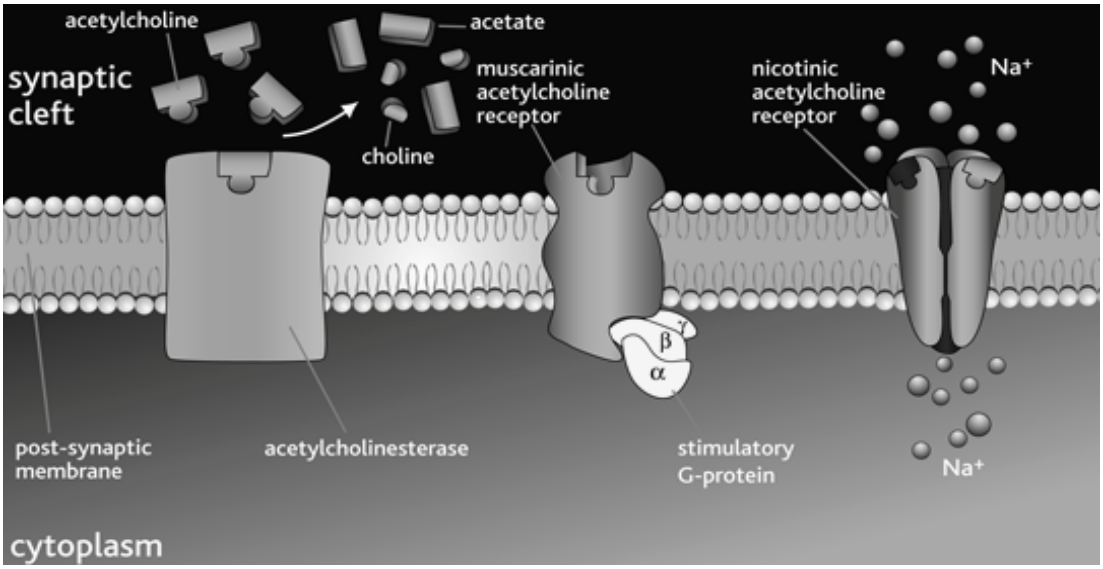


Figure 1: Action of acetylcholinesterase

OPCs inactivate AChE by phosphorylating the serine hydroxyl group located at the active site of AChE. The phosphorylation occurs by loss of an OP leaving group and establishment of a covalent bond with AChE. Once AChE has been inactivated, ACh accumulates throughout the autonomic nervous system, the somatic nervous system, and the brain, resulting in overstimulation of the muscarinic and nicotinic receptors.

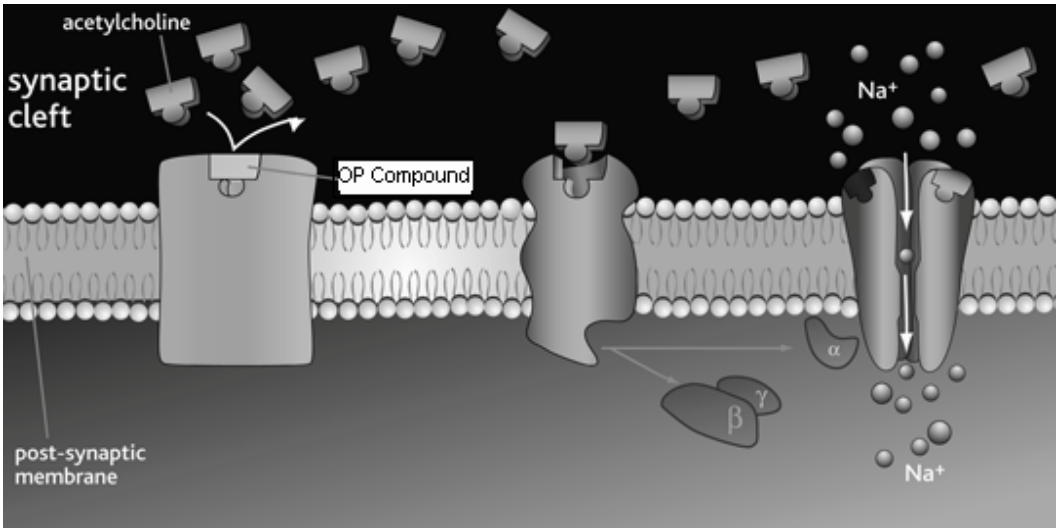


Figure 2: Inactivation of AChE by OPC and accumulation of ACh in the synapse. [22]

The preganglionic and postganglionic neurons in the parasympathetic nervous system release ACh. Postganglionic ACh acts on muscarinic receptors on the heart, eyes, glands, GI tract, and respiratory system. Somatic motor axons emerge from the spinal cord and directly innervate muscle cells at the neuromuscular junction, releasing ACh on nicotinic receptors. The brain and spinal cord both contain muscarinic and nicotinic receptors. Cholinergic pathways in the brain are associated with various behaviors and functions, including hunger, thirst, thermoregulation, respiration, aggression and cognition.

Once an OPC binds to AChE, the enzyme can undergo 3 processes:

(1) Endogenous hydrolysis of the phosphorylated enzyme by esterases ,

(2) Reactivation by a strong nucleophile such as Pralidoxime (2-PAM),

(3) Biological changes that render the phosphorylated enzyme inactive (ageing).

Although the splitting of the choline-enzyme bond in normal ACh metabolism is completed within microseconds, the severing of the organic phosphorus compound-enzyme bond can be prolonged.[23] In organic phosphorus compound poisoning, the complex becomes irreversibly bound during the next 24-72 hours when one of the R groups leaves the phosphate molecule. This step is termed ageing.[24] De novo synthesis of AChE is required to replenish its supply once ageing has occurred.

‘Aged’ AChE with its negatively charged phosphate can no longer be attacked by a negatively charged nucleophile, i.e. OH or an oximate group, and regeneration is no longer possible. Recovery can take up to 3 months for RBC and several weeks for plasma ChE.

The time it takes for ageing to occur varies according to the specific pesticide, but takes no longer than 48 hrs. Clinically, toxic effects of OP agents may persist for more than a week[25]. Oximes slow down “ageing” of the phosphorylated cholinesterase and binds to the OP agent, making it non reactive. This results in ChE regeneration and a rise in serum levels of ChE.

Common Organo-phosphate compounds and their brand names

Generic name	Brand name
Acephate	Acemil,Acet,Agrophate,Acetaf
Chloropyriphos	Agrofas 20, Chlorofos20,Daspan,Lethal
Cyclopyrifos	Duramet
Diazinon	Agroziron,Basudin, Bazanon,Tik 20
Dichlorvos	Agrovan76, Agro76, Cockroach killer
Dimethoate	Rogor,Primogor, Krogor, Corothate, Agrodimet 30, Tara 909
Ethion	Challenge, Demite, Dhanumit
Fenthion	Agrocidin, Baytex, Lebazate
Formothion	Anthio
Malathion	Agromal, Bharat, Celthion, Maladol
Methyl Parathion	Ant repellent, Folidol, Folidol-M,Parahit
Monocrotophos	Atom, Azodrin, Microphos, Macrophos
Phenthoate	Agrofen, Delsan, Guard
Phorate	Anuphorate, Croton, Dhan,Thimet
Phosmet	Phosmite
Profenfos	Carina, Curacrone, Polytrine
Quinalphos	Agroquin, Ekalux,Vikalux,Agroquinol, Bayrusil
Trichlorphon	Dipterex

TYPES OF CHOLINESTERASE (ChE)

Two types of Cholinesterases[19] have been distinguished according to their affinities for different substrates, endogenous such as acetylcholine, and exogenous such as acetyl-ß-méthylcholine, butyrylcholine and benzoylcholine.

Acetylcholinesterase:

Present in nervous tissue and erythrocytes, very quickly hydrolyzes acetylcholine and acetyl-ß-méthylcholine, but does not hydrolyze butyrylcholine. It is called true cholinesterase.

Butyrylcholinesterase:

Present in tissues such as heart and plasma, hydrolyzes acetylcholine, benzoylcholine, butyrylcholine but not acetyl-ß-méthylcholine. It is called pseudo-cholinesterase.

Types of Cholinesterase[19]

Properties	Red Blood Cell Cholinesterase	Butyrylcholinesterase or pseudo-cholinesterase
Advantage	Better reflection of synaptic inhibition	Easier to assay, declines faster
Site	RBC (reflects CNS gray matter, motor end plate)	CNS white matter, plasma, liver, pancreas, heart
Regeneration (untreated)	1%/day	25-30% in first 7-10 days
Normalization (untreated)	35-49 days	28-42 days
Use	Unsuspected prior exposure with normal plasma cholinesterase	Acute exposure
False depression	Pernicious anemia, hemoglobinopathies, antimalarial treatment, oxalate blood tubes	Liver dysfunction, malnutrition, hypersensitivity reactions, drugs (succinylcholine, codeine, morphine), pregnancy, genetic deficiency

In the acute phase of OP poisoning serum ChE activity is usually depressed within a few hours to few days and is also restored to normal levels quickly.[26] About 3% of the population have a genetic variation manifested by a serum cholinesterase deficiency. Pregnancy, acute (or) chronic inflammatory conditions, neoplasia, use of certain drugs (succinylcholine, codeine, and morphine), malnutrition and liver disease are conditions that also affect serum cholinesterase levels, but the depression caused by these conditions is not as great as that caused by organophosphate insecticide.

CLINICAL FEATURES[27]

Clinical effects of OPC poisoning are manifested through activation of the autonomic and central nervous systems and at nicotinic receptors on skeletal muscle.

Symptoms of acute organophosphate poisoning develop during or after exposure, within minutes to hours, depending on the method of exposure. All signs and symptoms are cholinergic in nature and affect muscarinic, nicotinic, and central nervous system receptors.

Signs and symptoms can be divided into three groups:

1. Muscarinic effects - Parasympathetic.
2. Nicotinic effects - Sympathetic and motor.
3. Central nervous system effects - M1 muscarinic receptor stimulation

1. Muscarinic Effects

Common manifestations include broncho-constriction with wheezing and dyspnea, cough, pulmonary edema, vomiting, diarrhoea, abdominal cramps, increased salivation, lacrimation, sweating, bradycardia, hypotension, miosis and urinary incontinence.

Some of these can be remembered by the acronym SLUDGE-**S**alivation, **L**acrimation, **U**rination, **D**iarrhoea, **G**astrointestinal distress and **E**mesis.

Bradycardia and hypotension occur in moderate to severe poisoning.

2. Nicotinic effects

Fasciculations, muscle weakness, and paralysis, hypertension, tachycardia, cardiac arrhythmias and conduction defects. ECG findings- sinus bradycardia, tachycardia, inter ventricular conductions delay, idioventricular rhythm, multiform premature ventricular extra systoles, ventricular tachycardia or fibrillations, torsades de pointes, prolongation of PR interval, ST-T wave changes, and atrial fibrillation.

3. Central Nervous System (CNS) effects

Restlessness, headache, tremor, drowsiness, delirium, slurred speech, ataxia and convulsions. Coma supervenes in late stages.

It is important to note that :

- In any given case there may be tachy- or bradycardia, hypo- or hypertension.
- Miosis being a very characteristic feature may not be present in all cases. In fact mydriasis may be present in the initial stages and treatment should not be deferred if there is no miosis. Blurred vision may persist for months.
- Ocular absorption may lead to systemic toxicity and miosis may be present in spite of systemic treatment and may require topical atropine instillations.
- Exposure to OPC vapors produces immediate symptoms of mucous membrane and upper airway irritation and bronchospasm, followed by systemic symptoms if patients are exposed to significant concentrations.
- While respiratory failure is the commonest cause of death other causes may contribute including hypoxia due to seizures, hyperthermia, renal failure and hepatic failure.
- Patients with OPC poisoning and QTc prolongation have more chances of developing respiratory paralysis[28] than those with normal QTc interval. Patients who develop PVCs are more likely to develop respiratory failure than patients who do not develop PVCs.
- Aspiration of preparations containing hydrocarbon solvents may cause potential fatal lipoidal pneumonitis.
- Parathion is sometimes associated with haemorrhagic pancreatitis which can be fatal. Diazinon has also been implicated to cause pancreatic damage.

The critical symptoms in management are the respiratory symptoms.[29] The primary cause of death is respiratory failure. Sufficient muscular fasciculations and weakness are often observed as to require respiratory support; respiratory arrest can occur suddenly. Likewise, bronchorrhea and bronchospasm may often impede efforts at adequate oxygenation of the patient. Bronchospasm and bronchorrhea manifest with tightness in the chest, wheezing, productive cough, and pulmonary edema. A life threatening severity of poisoning is signified by loss of consciousness, incontinence, convulsions, and respiratory depression and there usually is a secondary cardiovascular component.

The classic cardiovascular sign is bradycardia which can progress to sinus arrest. However, this may be superseded by tachycardia and hypertension from nicotinic (sympathetic ganglia) stimulation.[30] Toxic cardiomyopathy has been a prominent feature of some severe organophosphate poisoning.

Muscle twitching, weakness, tremor, in-coordination, vomiting, abdominal cramps, and diarrhoea all signal worsening of the clinical state.

In recent works, it has been reported that children, particularly those under nine years of age, are unlikely to develop classic “muscarinic” signs of OP poisoning. More often than not, younger children manifest “nicotinic” signs of poisoning. The most common features in pediatric poisoning are CNS depression and hypotonia.

***Intermediate syndrome* (IMS)[31]**

This syndrome occurs after resolution of the acute cholinergic crisis, generally 24-96 hours after exposure. IMS lacks muscarinic symptomatology, and appears to result from a combined pre- and post-synaptic dysfunction of neuromuscular transmission. The most common compounds involved in this syndrome are Methyl parathion, Fenthion and Dimethoate.

Main features are motor cranial nerve palsies, muscle weakness and paralysis characterized by weakness of neck flexors and proximal limb muscles and acute respiratory paresis. Paralytic signs include inability to sit up or lift the neck, ophthalmoparesis, slow eye movements, facial weakness, and difficulty in swallowing, limb weakness, areflexia, respiratory paralysis followed by death.

It is usually due to suboptimal administration of oximes or inadequate ventilatory support. Several investigators have suggested development of intermediate syndrome due to various causes:

1. Inadequate Oxime therapy,
2. Dose and route of exposure,
3. Chemical structure of Organophosphates,
4. Timing of therapy.

Management of intermediate syndrome is supportive. Measures as oximes and atropine are not found useful. Recent study in India shows one third of all poisoning cases admitted in major hospital developed intermediate syndrome.

Organophosphate-Induced Delayed Polyneuropathy (OPIDP)[32]

A *delayed syndrome* occurs 1 to 4 weeks after poisoning due to nerve demyelination and it is characterized by either flaccid paralysis of distal limbs with atrophy or spasticity and ataxia. Relative sparing of the neck muscles, cranial nerves, and proximal muscle groups characterize OPIDP. OPIDP is motor predominant, and pure sensory neuropathy do not occur .A mixed sensory-motor neuropathy usually begins in the legs causing burning sensation or tingling and then weakness. This syndrome also does not respond to oximes and atropine. Severe cases progresses to respiratory failure and death. The delayed neuropathy is most often permanent. The mechanism appears to involve phosphorylation of enzyme Neuropathy Target Esterase (NTE) in peripheral nervous tissue and results in a “dying-back” pattern of axonal degeneration. Recovery can take up to 12 months.

Classification of Severity in Organophosphorus Poisoning (NAMBA)

Type of poisoning	**Clinical definition**
LATENT POISONING NAMBA – I	No clinical manifestations, Diagnosis depends on the estimation of serum ChE activity which is inhibited by 10-50%
MILD POISONING, NAMBA –II	The patient can walk but complains of Fatigue, headache, dizziness, numbness of extremities, nausea and vomiting, excessive sweating and salivation, tightness in chest, abdominal cramps or diarrhoea; serum ChE activity is 20-50% of normal value.
MODERATEPOISONING NAMBA – III	The patient cannot walk and there is generalized weakness, speaking difficulty, muscular fasciculations, miosis and severe symptoms described above; serum ChE activity is 10 -20% of normal value.
SEVERE POISONING NAMBA IV	Unconsciousness, marked miosis and loss of pupil reflex to light, muscular fasciculations, flaccid paralysis, secretions from the mouth and nose, moist rales in the lungs, respiratory difficulty and cyanosis; serum ChE activity is lower than 10% of normal value.

INVESTIGATORY MODALITES:

1. Cholineesterase levels:

Reduction of plasma pseudocholinesterase and/or RBC acetylcholinesterase enzyme activities are generally available biochemical indicators of excessive organophosphate absorption. Certain organophosphates may selectively inhibit either plasma pseudocholinesterase or RBC acetylcholinesterase.[33] The AChE level can vary widely from person to person. A 50% reduction in ChE activity from the baseline may result in acute cholinergic symptoms of organophosphate exposure. These values differ among laboratories, and the range is very wide, with a 30% spread.

Although RBC and plasma (pseudo) cholinesterase levels can both be used, RBC cholinesterase correlates better with CNS acetyl cholinesterase (AChE) and is, therefore, a more useful marker of organophosphate poisoning.

- Monitoring serial levels can be used to determine a response to therapy.
- Cholinesterase levels do not always correlate with severity of clinical illness.
- Falsely depressed levels of erythrocyte cholinesterase can be found in pernicious anemia, hemoglobinopathies, use of antimalarial drugs, and oxalate blood tubes.

2) Serum electrolytes, creatinine and urea:

To assess the degree of volume depletion in the presence of muscarinic secretory losses from the pulmonary and alimentary tracts.

3) Blood Urea Nitrogen (BUN) Monitoring:

To predict the development of relapse in OP poisoning. Elevation from its normal range [8-20 mg/dl] is seen in acute poisoning.[34]

4) Arterial Blood Gas (ABG) analysis:

To assess the degree of hypoxia and hypercapnia in the presence of respiratory distress from pulmonary congestion.

5) Serum glucose:

Hyperglycemia has been reported in many studies. The increase in serum glucose is due to secondary release of catecholamines from the adrenal medulla.[35]

6) Leukocyte Count:

Leucocytosis is a common finding in OP intoxication. It helps to assess the prognosis and efficiency of treatment.[36]

Imaging Studies

Chest X-ray: For evaluating pulmonary edema (or) congestion.

CT/USG Abdomen: to evaluate the pancreatic status.

Electrocardiogram (ECG)

Useful for evaluating the arrhythmias including atrial fibrillation, ventricular tachycardia and torsades de pointes (or) QT prolongation.[37]

Amylase:

Although many tissues synthesize amylase, most of the serum activity originates from the pancreas (approximately 40%) and the salivary glands (approximately 60%). Electrophoresis shows that serum amylase is of two main types:

(1) P-type amylase from the pancreas, and

(2) S-type amylase from the salivary glands.

Fallopian tube secretions, tears, breast milk and sweat have amylases with a similar electrophoretic mobility of salivary isoamylase. However, the salivary glands account for almost all of the S-type isoamylase. Pancreatic amylase enters the blood through an unknown pathway and has a serum half-life of about 2 hours. Although the major portion of serum amylase and other pancreatic enzymes is probably cleared by the reticulo-endothelial system, about one fourth of serum amylase is excreted in its intact form by the kidney.

Hyperamylasemia is nonspecific because it occurs in many conditions other than acute pancreatitis. One half of all patients with a serum amylase elevation may not have pancreatic disease.[38] In acute pancreatitis, the serum amylase concentration is usually more than two to three times the upper limit of normal; it is usually less than this with other causes of hyperamylasemia.[39] However,

this level is not an absolute discriminator. Thus, an increased serum amylase level supports rather than confirms the diagnosis of acute pancreatitis. In addition, some individuals have persistent hyperamylasemia without clinical symptoms. This situation has been reported to be due to macroamylasemia or familial pancreatic hyperamylasemia.[40]

Metabolic clearance of serum amylase :

The exact mechanisms of serum amylase metabolism are still not fully understood. Humans who have had a nephrectomy or those who have renal insufficiency have average serum amylase levels 50% higher than healthy individuals. Therefore, kidneys can be assumed to play a major role in amylase metabolism. However, kidney is not the sole organ responsible for amylase clearance in humans. The extra renal mechanisms of amylase clearance have not been defined. Because of the high serum amylase levels also observed in hepatic necrosis and cirrhosis, liver is thought to play a role in amylase metabolism.

CAUSES OF HYPERAMYLASEMIA

Pancreatic Disease

1. Acute or chronic pancreatitis
2. Pancreatic pseudocyst
3. Pancreatic trauma (blunt trauma, ERCP related)
4. Pancreatic carcinoma

Non pancreatic Disease

- Salivary gland lesions
- Renal insufficiency
- Tumor (lung, esophagus, ovary, breast)
- Biliary tract disease (cholecystitis, choledocholithiasis)
- Perforated peptic ulcer
- Intestinal obstruction or infarction
- Postoperative hyperamylasemia
- Peritonitis
- Acidosis
- Ruptured ectopic pregnancy, fallopian or ovarian cysts, and salpingitis
- Burns
- Pregnancy
- Pneumonia, cerebral trauma, burns, abdominal aortic aneurysms ,
- Anorexia nervosa and bulimia
- Organophosphate poisoning.
- Renal transplantation
- Drugs (morphine, codeine)

EFFECT OF ORGANOPHOSPHORUS COMPOUND ON PANCREAS:-

Various studies show that there is increased incidence of Pancreatitis and its related complications after consumption of organophosphorus compound when compared to general population. There is elevated serum Amylase level in these patients.

Though the exact mechanism for its occurrence is not known , the following mechanisms have been suggested .

a) OP insecticides increase the intraductal pressure and exocrine pancreatic flow. The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could be due to direct cholinergic hyper stimulation of pancreatic acinar and ductal cells .
b) Experimental data supports the view that these organophosphate compounds cause a functional ductal obstruction at the same time as stimulation of pancreatic exocrine secretion.
c) There is pancreatic interstitial edema, acinar cell vacuolization, hyperamylasemia and hyperlipasemia following ingestion of OP poisoning.

TREATMENT OF OPC POISONING

Organophosphate poisoning is a serious condition that needs rapid diagnosis and intensive care support. Patients who receive appropriate treatment immediately recover from acute toxicity.

PROTECTION:

- OPC intoxicated patients serve as a source of poisoning for the health-care professionals by direct contact.
- Hence health-care professionals are required to wear PPE (personal protective equipments) at least until the patient is externally decontaminated.[41]

DECONTAMINATION:

- Remove patient from the source of poisoning.
- All clothing, especially leather should be removed and discarded in a ventilated area.
- Skin and hair decontamination should be done with water irrigation and can be enhanced by using alcohol-based soaps.
- Water irrigation should be used for ocular decontamination.
- Gastric lavage is indicated in stable patients who have ingested contaminated fluids.
- All the lavaged/aspirated fluids should be safely discarded.

The main – stays of treatment are,

- Supportive care
- Atropine
- Oximes
- Benzodiazepines

SUPPORTIVE CARE:

* Gastric lavage
* Air way control
* Oxygenation
* Ventilation and
* Seizure management.

STABILIZATION:

- ABCs: Have a low threshold for early intubation in order to obtain airway protection.
- Avoid mouth-to-mouth resuscitation for the risk of contamination.
- Start IV fluids as an initial bolus dose of 20ml/kg[42].

ATROPINE:

Atropine is an anti-muscarinic agent which competes with ACh for receptor binding.

Targeted End – Points of Atropinisation.[41]

- Clear lungs(i.e.) drying of bronchial secretions with normalized oxygen saturation

- Dry axillae
- Systolic BP > 80mm Hg.
- Heart rate > 80 /min
- No miosis

The initial adult dose is 1 to 3 mg IV bolus. Then titrate[43] according to persistence of bronchorrhea by giving double the previously used dose every 5 minutes until atropinization achieved. The initial pediatric dose is 0.02mg/kg IV. Titrate as in adults. Once the patient is stabilized an infusion of atropine should be started with 10% to 20% of the initial atropinization dose per hour and should be held once anti-cholinergic effects occur.

- NOTE: Atropine has no effect on neuromuscular junctions, therefore Pralidoxime should be added as early as possible in order to reverse muscle weakness.

Atropine Toxicity:-

Excess atropine can cause atropine toxicity characterized by confusion, agitation, atropine induced hyperthermia and cardiac arrest.

Glycopyrrolate

It has been studied as an alternative to atropine and found to have similar outcomes using continuous infusion. Ampoules of 7.5 mg of glycopyrrolate were added to 200 ml of saline and this infusion was titrated to the desired effects of dry mucous membranes and heart rate above 60 beats/min. The other apparent advantage to this regimen was decreased tendency to develop

respiratory infections. This may represent an alternative when there is a concern for respiratory infection due to excessive secretions, and in the presence of altered level of consciousness where the distinction between atropine toxicity or relapse of organophosphate poisoning is unclear.[44]

OXIMES:

Category: Cholinesterase reactivators.

Oximes are effective in treating nicotinic symptoms by reversing the phosphate – ester bond formed between the OP and acetyl cholinesterase and this reactivates the enzyme. It also prevents subsequent binding of insecticides to the AChE and accentuates therapeutic effects of atropine.

- Pralidoxime forms a complex with OPCs that are bound to AChE. The Pralidoxime-OP complex is then released from the enzyme and thus regenerates AChE function.
- Once the AChE bound OPCs start ageing, Pralidoxime is rendered ineffective. Therefore, early start of Pralidoxime therapy is crucial.
- Pralidoxime also binds to free OPCs and thus preventing further AChE binding.
- Adult Dosing used to be administered in boluses over given time. New evidence, is however recommending infusion regimens. 1-2g of Pralidoxime in 100ml NS IV over 20minutes, then infusion at 500mg/hour. [45,46]
- Pralidoxime use longer than 24 hours is indicated if unaged OPCs are redistributed from fat tissues. In such cases infusions should be continued

until patient remains symptom-free for atleast 12 hours without additional atropine doses, or until patient is extubated.

- Cardiac and respiratory failures have been reported after administration of Pralidoxime.[47]
- Though Pralidoxime might not be effective in all cases of OPC poisoning due to the ageing effect, it is still recommended to be used routinely in order to decrease the total atropine requirements.

BENZODIAZEPINES:

- Benzodiazepines are the first-line agents for OPC induced seizures.[48]

STUDIES ON EFFECT OF OP COMPOUNDS ON SERUM AMYLASE LEVELS:

- A prospective study was undertaken in PGIMER,Chandigarh, India between July 2001-June 2005[49] to find the incidence of hyperamylasemia and acute pancreatitis in patients with OP poisoning. Of the 79 patients studied, patients who presented with cholinergic crisis had >50% reduction in serum cholinesterase levels and serum Amylase was found to be elevated (> 200 S.U) in 37 patients (46.95%). Among them in three patients it was 800 S.U. Not all patients showed radiological evidence of acute pancreatitis. Except for Fenthion, significant persistent elevation of amylase was not observed. Elevated amylase levels were constantly associated with polymorpho leucocytosis, hyperglycemia and elevated transaminase levels were noted. It has been concluded that mild elevation of serum Amylase is common in

patients with OP poisoning, however acute pancreatitis is rare.

- A retrospective study analysis of medical records of 121 patients with the diagnosis of OP poisoning over three years was done in Veterans general hospital, National Yang- Ming University in 1998. Serum amylase, pancreatic amylase, salivary amylase, lipase and cholinesterase levels and the clinical manifestations were analyzed. It was observed that 44 patients (36%) had hyperamylasemia (Amylase >360 U/L). Lipase was measured in 28 patients with hyperamylasemia ; nine of 28 had hyperlipasemia (Lipase > 380 U/L). The finding of hyperamylasemia was closely related to clinical severity and presence of shock. Few patients who had elevated lipase levels with hyperamylasemia had shown features of acute pancreatitis and thus looking for elevated p-lipase may be a better marker than p-amylase to diagnose painless acute pancreatitis and elevated p-amyalse levels alone is not indicative of acute pancreatitis.
- In an experimental study done at Department of surgery, University of Minnesota Medical School, Minneapolis[50], the effects of OPC in-vitro on pancreatic exocrine function was studied and it was found that the canine pancreas pretreated with Iso-OMPA showed a 42-87% greater release of amylase in response to acetyl-choline, than was seen in receiving acetylcholine alone.
- Study done in Dept. of Anaesthesiology, Afyon Kocatepe University, Turkey[51] revealed that high dose atropine that is administered for 24 hours or the first 4 hours after intoxication prevented severe pancreatitis. This was

done only for Fenthion-induced pancreatitis & its influence should be studied for other organophosphates in humans.

- A prospective study was done by the Department of Internal Medicine,University of Yuzuncu Yil,Medical faculty,Van,Turkey[52] in 2002 to find the prevalence of pancreatitis in OP poisoning. Four of the total 47 patients with acute OP poisoning had obviously elevated Amylase and Lipase levels (Amylase> 300 U/L; Lipase >60 U/L). Only two of the patients with Amylase levels between 100 and 300 U/L had elevated levels of Lipase. None of the patients with normal Amylase levels had elevated levels of Lipase. A total of 12.76% was diagnosed as having acute Pancreatitis. It was concluded that acute Pancreatitis is not a rare complication of Organophosphorus poisoning. In order to improve the outcome of OP poisoning early diagnosis of acute pancreatitis is important and serum Amylase and Lipase levels should be routinely considered carefully.
- A retrospective study of OP poison in intensive care unit was performed to analyze the incidence of respiratory failure by Department of Anesthesiology & Critical care medicine, Kyodo general hospital,Ibaraki Japan[53]. Of the 32 op poisoning Patients, 16 developed respiratory failure and received ventilatory support. An increase in plasma Amylase above the normal range was found in patients who developed respiratory failure. Thus in OP poisoning, the elevation of Amylase levels was predictive of subsequent respiratory failure.

AIM OF THE STUDY

1) To estimate serum Amylase and serum cholinesterase levels in acute organophosphorus compound poisoning.
2) To compare its levels with control group.
3) To compare the serum levels of amylase and cholinesterase in patients with OPC poisoning and their association with clinical severity.

MATERIALS AND METHODS

Subjects:

Patients presenting with Organophosphorus poisoning were the study subjects.

Study design:

A cross - sectional study.

Ethical committee approval:

The Ethical committee approval was obtained to carry out the study in the hospital. Consent obtained.

Study setting:

Tirunelveli medical college hospital.

Study duration:

Dec 2010– Oct 2011

Materials:

A total of 185 patients with organophosphorus compound poisoning admitted to the hospital during the study period, out of which 62 were included in the study.

Controls:

40 healthy (age matched) individuals were kept as control.

Study criteria:

Inclusion criteria:

Patients with a history of exposure to OP poison were the study subjects.

Exclusion criteria:

- Patients with indication of exposure to an entirely different poison other than OPC
- Patients with double poisoning
- Patients who have consumed poison along with alcohol
- Patients who are chronic alcoholics
- Patients with history suggestive of gall stone disease
- History suggestive of parotid gland disease
- Patients with history of lipid disorders
- Patients with history of renal or hepatic disease
- Pregnancy
- H/o abdominal trauma, Endoscopic Retrograde Cholangiopancreatography (ERCP)
- History of intake of drugs likely to produce pancreatitis-Azathioprine
- 6-Mercaptopurine, Thiazides, Frusemide, Pentamidine, Steroids, valproate Sulphonamides.

Study protocol:

Patients admitted in Tirunelveli Medical College & Hospital during the study period were included in the study group. A previously designed proforma

was used to collect the demographic and clinical details of the patients.

Collaborating department:

Department of Biochemistry, Tirunelveli Medical College, Tirunelveli.

Exposure assessment:

The following parameters were analyzed for association with OP pesticide exposure.

- **Demography**

  Age

  Sex

  Time of Admission

  Economical Status

  Familial Status

  Reason for consumption

- **Poison Particulars**

  Severity grade

  Symptoms after consumption

  Immediate steps taken after OP exposure

- Biochemical evaluation which includes Serum Amylase, serum cholinesterase, Blood glucose, urea, creatinine and Liver function tests.
- Clinical Outcome, Clinical Presentations

  Pupil size, Pulse rate/min, Blood pressure, Respiratory rate/min, Secretions.

Sample collection:

62 Patients satisfying the inclusion criteria were selected for the study. About 3 ml of venous blood were collected in two occasions from each subject first sample, at the time of admission (Sample I) and next sample after 24 hours (Sample II). The samples were centrifuged at 3000 rpm for 15 minutes.

The supernatant serum was separated and freezed. Serum Amylase was estimated with the help of kit manufactured by ERBA diagnostics by using CNP-G3 method. Normal range: up to 80u/l.

Serum cholinesterase is measured in our lab by the new DGKC method with the use of an auto-analyzer. The normal range provided by our lab is,

Females: 3930-10800 U/L

Males : 4620-11500 U/L

Limitations of this study:

a) In this present study, patients were not subjected to CT / USG Abdomen because the study was limited to serum Amylase only.
b) Autopsy study of pancreas was not done in the view of social limitation.
c) Subsets of Amylase such as pancreatic and salivary Amylase was not estimated due to laboratory constraints.
d) Urinary Amylase was not estimated due to technical limitations.
e) Other biochemical parameters related to pancreatic involvement was not attempted due to financial constraints.

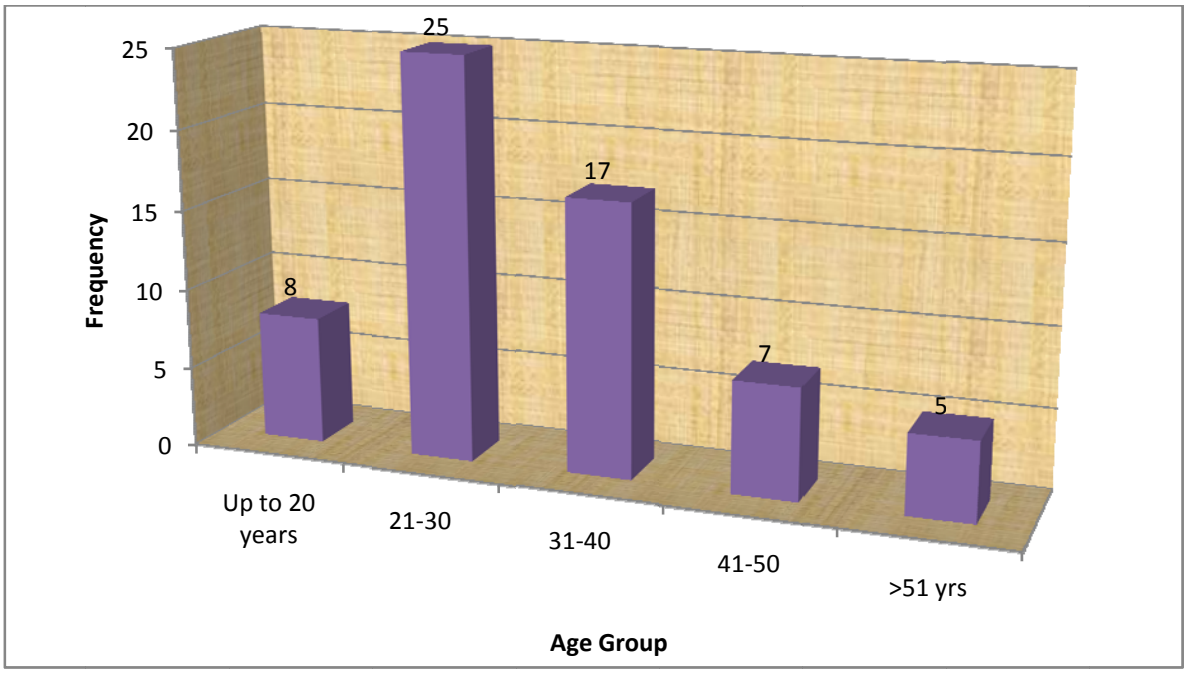
STATISTICAL ANALYSIS:

Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002).

Using this software, frequencies, percentages, means, standard deviations, chi square test, paired ‘t’ test, unpaired ‘t’ test and association were applied. A 'p' value less than 0.05 is considered significant.

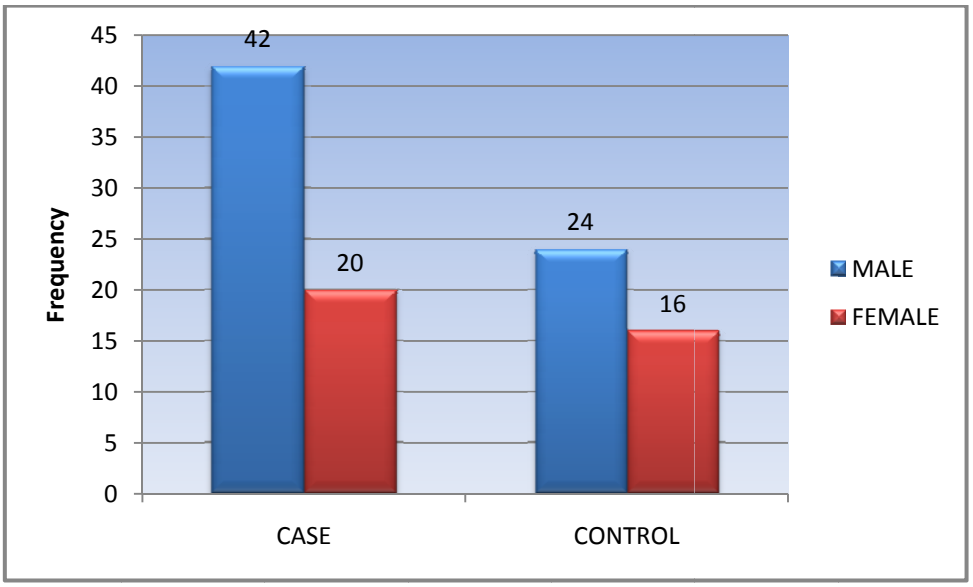
OBSERVATIONS AND RESULTS

FIG 1: AGE DISTRIBUTION AMONG OP POISONED CASES



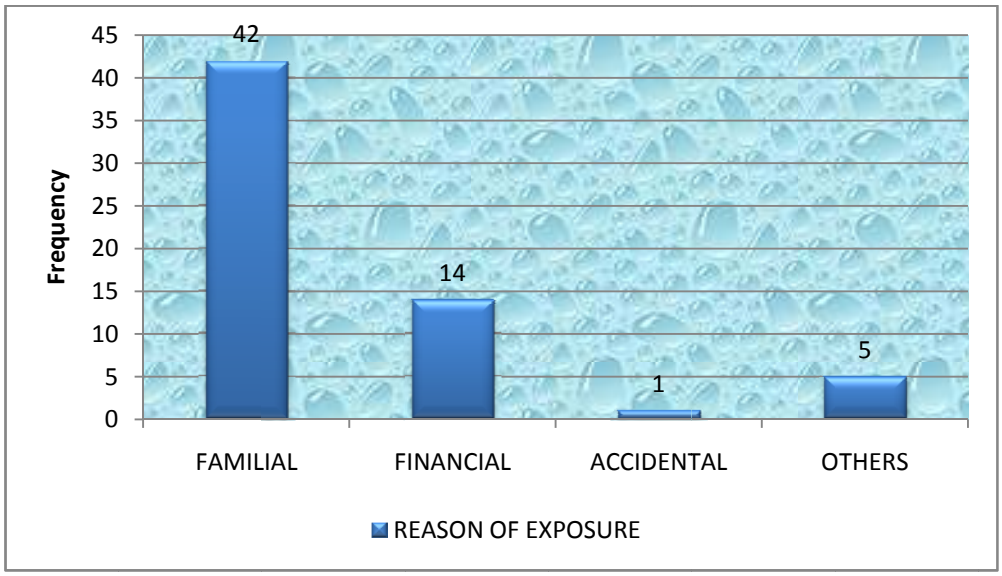
Age wise distribution shows that majority of our study population belongs to the age group of 21-30 years (n=25) followed by the people of age group 31-40 years (n=17).

FIG 2: SEX DISTRIBUTION



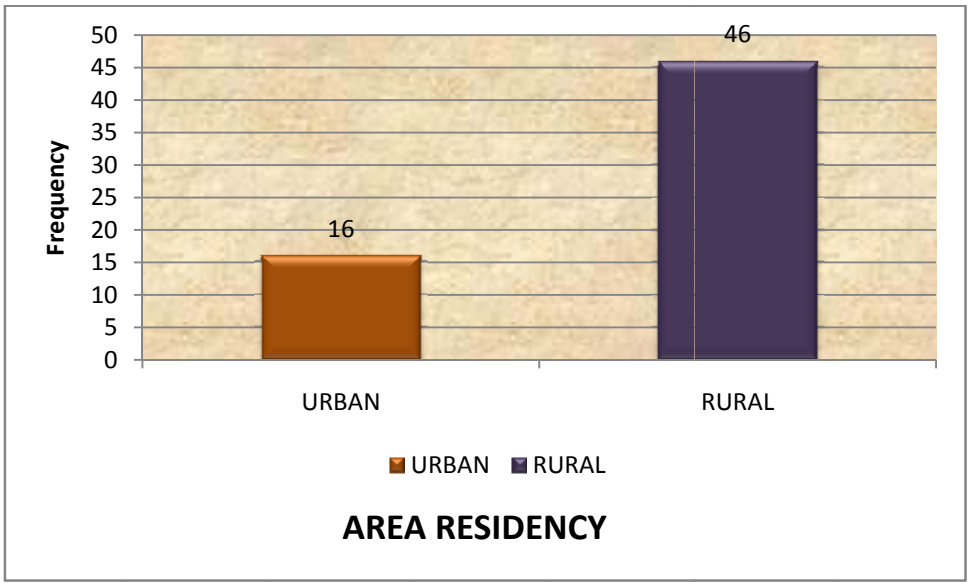
The data from our study shows predominance of poisoning in the male population (67.37%) when compared to the female population (32.3%)

FIG 3: REASONS FOR POISONING



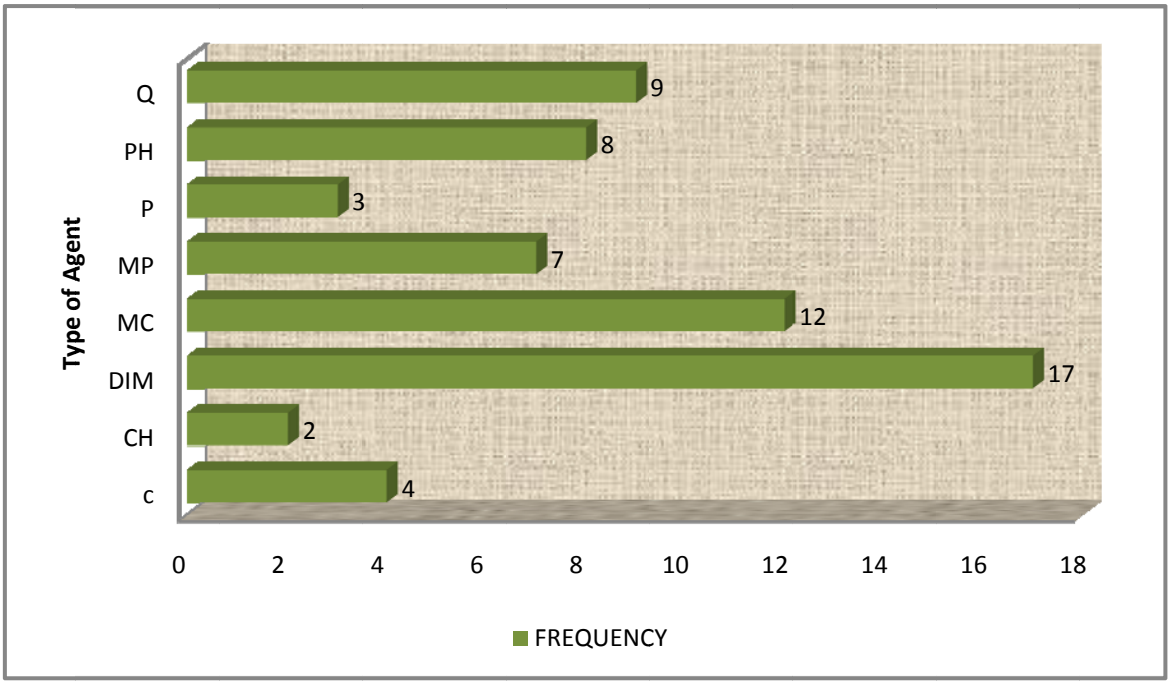
Familial problems are the main reason for poisoning with OPC followed by financial problems and other reasons like chronic illness, love failure, work related stress. Out of the total 62 cases studied, only 1 case was of accidental poisoning (occupational exposure).

FIG 4: AREA OF RESIDENCY



From our study, we found that OPC poisoning is more prevalent among the rural population 74.2% (n=46) than the urban population 25.8% (n=16).

FIG 5: AGENT OF POISONING



- Q - QUINOLPHOS
- PH- PHORATE
- P- PARATHION
- MP- METHYL PARATHION
- MC- MONOCHROTOPHOS
- DiM- DIMETHOATE
- CH- CHLORPYRIFOS
- C- CYCLOPYRIFOS

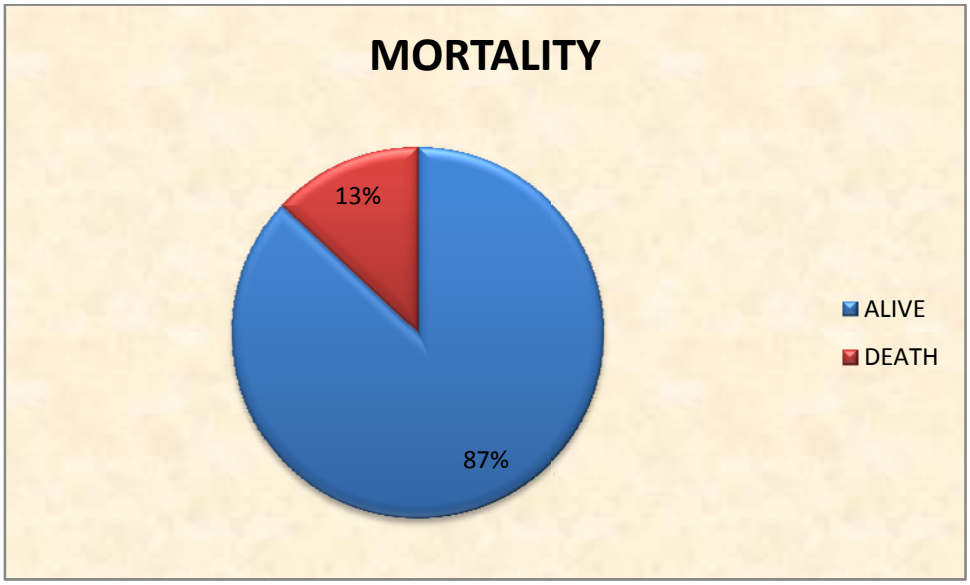
Our study shows that the chemical Dimethoate(DiM)(n=17) is the most common agent of poisoning followed by Monochrotophos(MC) and Quinolphos(Q).

TABLE 1: CLINICAL FEATURES

S. No	Clinical features	No of Cases	Percentage (%)
1.	Pinpoint pupil	40	64.5
2.	Depressed mental status	12	19.4
3.	Secretions (45) i) Mild ii) Moderate iii) Severe	 23 20 2	 37.1 32.2 3.2
4.	Fasciculation	33	53.2
5.	Heart Rate Bradycardia	 20	 32.3
6.	Hypotension	5	8.1
7.	Convulsions	5	8.1
8.	Respiratory Failure	23	37.1

Analyzing the occurrence of symptoms in this study, we found that secretions(72.5%) and pin-point pupil(64.5%) are the most common symptoms and hypotension(8.1%) and convulsions(8.1%) being the least common symptoms occurring in poisoning.

FIG 6: MORTALITY



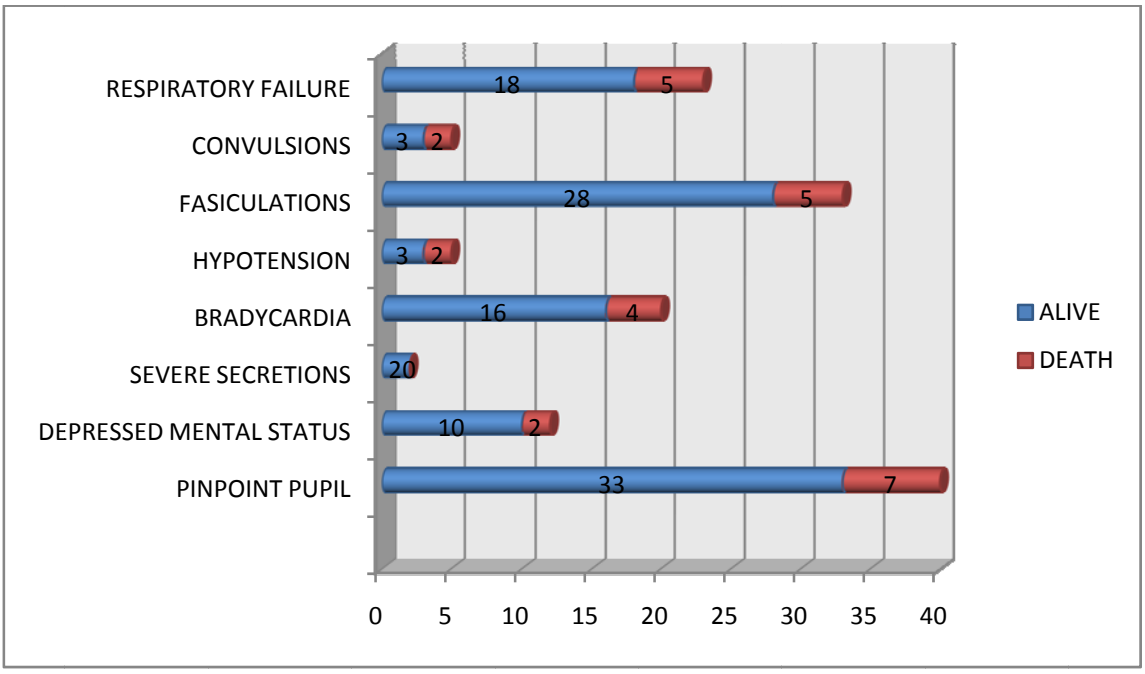
Out of the 62 patients we studied, the mortality rate was 13% (n=8).

TABLE 2: LAB PARAMETERS

S. No	Parameter	Cases		Controls		'p'value
		Mean	S.D.	Mean	S.D.	
1.	Serum amylase–I (unit/L)	154.61	121.52	43.95	23.19	< **0.01** **Significant**
2.	Serum cholinesterase-I (unit/L)	3428.71	1943.56	5449.25	1284.32	< **0.01** **Significant**
3.	Total WBC count (cells/cu.mm)	8503.23	3566.97	7725.00	2601.85	0.237
4.	Blood sugar (mg %)	125.94	36.16	121.03	29.21	0.473
5.	Blood urea (mg %)	27.02	7.43	28.83	8.83	0.268
6.	Serum Creatinine (mg %)	0.92	0.21	0.96	0.24	0.459

Compared to control group of our study, the serum amylase and serum cholinesterase values of the cases show significance ($p<0.05$), suggesting association between the enzyme levels and the severity.

FIG 7 : CLINICAL FEATURES AND OUTCOME



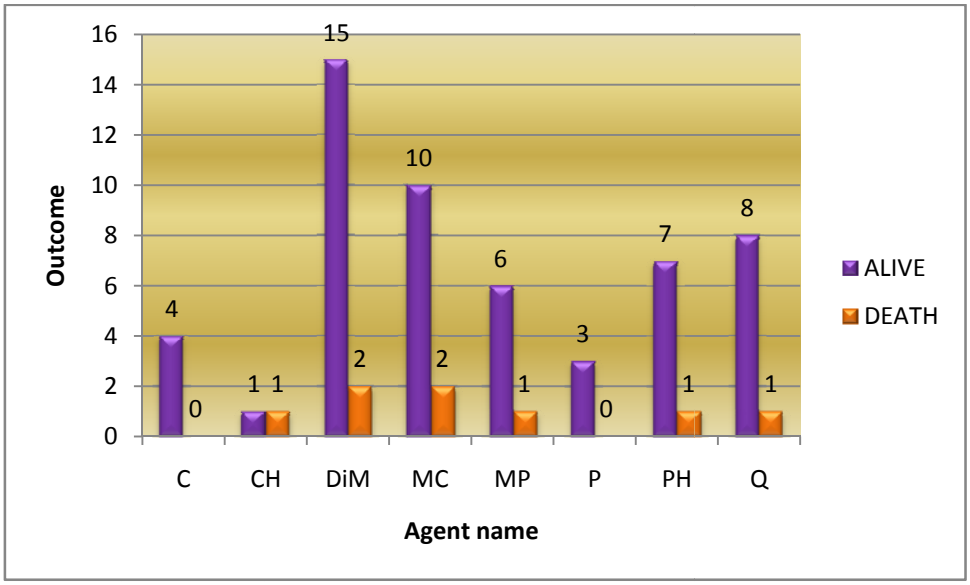
From our observation, more number of patients with pinpoint pupil at presentation have higher mortality followed by patients with fasciculation and respiratory failure.

TABLE 3: AMYLASE LEVELS, CHOLINESTERASE LEVELS

S. No	Lab parameter	Sample I- [Taken at the time of admission]		Sample II [taken 24 hrs after admission]		'p'
		Mean	SD	Mean	SD	
1.	Serum Amylase	154.61	121.51	129.27	92.34	<0.001
2.	Serum cholinesterase	3428.71	1943.56	3336.94	1822.54	0.555

In our study, the serum amylase level at the time of admission is higher than its level observed 24 hours after admission. This is statistically significant.

FIG 8: POISONING AGENT AND THEIR MORTALITY



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- MC- MONOCHROTOPHOS
- DiM- DIMETHOATE
- CH- CHLORPYRIFOS
- C- CYCLOPYRIFOS

Based on this study results Dimethoate and Monochrotophos are the compounds with higher mortality rate compared to others.

TABLE 4: CLINICAL FEATURES AND AMYLASE LEVEL

S. No	Clinical features	Serum Amylase I		'p' value
		Normal	Elevated	
1.	Pinpoint pupil	14	26	0.067
2.	Depressed mental status	2	10	**0.035 (significant)**
3.	Secretions	17	28	**0.048 (significant)**
4.	Bradycardia	4	16	**0.010 (significant)**
5.	Hypotension	1	4	0.268
6.	Convulsions	1	4	0.268
7.	Fasciculation	10	23	**0.025 (significant)**
8.	Respiratory Failure	5	18	0.08

From observing the above data, we found out that patients with symptoms of bradycardia, fasciculations, depressed mental status and secretions have significant rise in serum amylase levels.

TABLE 5: CLINICAL FEATURES AND SERUM CHOLINESTERASE LEVEL

S. No	Clinical features	Serum Cholinesterase I		'p' value
		Depressed	Normal	
1.	Pinpoint pupil	29	11	**0.006 (significant)**
2.	Depressed mental status	10	2	0.1
3.	Secretions	31	14	0.051
4.	Bradycardia	17	3	**0.005 (significant)**
5.	Hypotension	5	0	0.055
6.	Convulsions	5	0	0.055
7.	Fasciculation	25	8	**0.006 (significant)**
8.	Respiratory Failure	19	4	**0.005 (significant)**

By observing the study results, we found that there is significant decrease in serum cholinesterase level in patients with respiratory failure, bradycardia and fasciculations.

TABLE 6: OUTCOME AND AMYLASE LEVELS

S. No	Serum Amylase	Outcome		"p" value
		Alive	Death	
1.	Normal	22	4	0.620
2.	Elevated	32	4	
3.	Total	54	8	

Observing the results from our study, we can see that there is no significant correlation between the serum amylase level and the outcome.

TABLE 7: OUTCOME AND SERUM CHOLINESTERASE LEVEL

S. No	Serum Cholinesterase	Outcome		'p' Value
		Alive	Death	
1.	Normal	24	1	0.270
2.	Depressed	30	7	
3.	Total	54	8	

Our study reveals no significant association between the serum cholinesterase level and outcome.

DISCUSSION

As discussed in the literature, OPC poisoning is a common presentation in the Intensive Care Unit (ICU) setup and one with high mortality, much of which can be reduced with proper treatment. Defining the factors that affect the prediction of mortality and prognosis in OP poisoning will help guide follow-up and treatment in the intensive care unit. Serum Amylase and ChE estimation are helpful tools in assessment and management of these patients. Here, we perform a critical analysis of the observations of our study comparing it with other Indian and foreign studies.

Age wise distribution

By analyzing the data of our study, we found that poisoning is more common among the people in the age group of 21-30(40.3%) years followed by the people of age group 31-40 years(27.4%).These are consistent with the findings of Muhammet Guven et al[36] and AM Saadeh et al[37], where the mean ages were 24.1 and 23.95 respectively. Familial problems are the main reason for poisoning in this age group followed by financial problems and other reasons like love failure, work related stress.

Sex wise distribution:

In our study, males were more affected (67.7%) than the females (32.3%). Similar observations were made by Dalal et al[54]. Males constituted 63% of cases of poisoning and still higher incidence was observed by Agarwal et al i.e. 72% cases of poisoning in males.

Geographic distribution:

Our study showed a predominance of rural population consuming OPC. This is consistent with Girish Thunga et al[55](2008) who reported 66.67% and Dalal et al(1998)70.5%.Obvious reasons being the easy availability of pesticides to the rural population.

Compound:

Our study showed that the chemical Dimethoate (27.4%) is the most common agent of poisoning followed by Monochrotophos (19.4%) and Quinolphos(14.5%). A similar study in South India by Rao et al[56] (2005) showed that majority of the cases were admitted due to ingestion of Monocrotophos.

Clinical symptoms

Both the present study, and the study by Mahdi Balali-Mood et al[57], found association between the severity of poisoning and clinical manifestations.

The most marked muscarinic signs in our study population were, miosis (64.5%) and excessive secretions (72.5%).The most prominent of the nicotinic effect is muscular end plate block, resulting in muscle weakness and fasciculations (53.2%) and respiratory failure(37%). The CNS symptoms, like depressed mental status was found in (19.3%) patients. Similar findings have also been reported by Murat Sungur et al[35]. The results of prospective observational study[58] done at Dept.of chest medicine, King Edward memorial hospital Mumbai supports our observation that clinical features of miosis,

unconsciousness and fasciculations are strong predictors of the severity of poisoning& ultimately the requirement for ventilator support.

Biochemical evaluation

The biochemical (Blood sugar, Serum creatinine & urea) results have not shown much variation from the normal levels in our study. There is no statistical significance found for these lab parameters. This was also indicated by Mahdi Balali-Mood et al[57] .But Singh et al(PGIMER) reported significant hyperglycemia with OPC poisoning. Hyperglycemia is attributed to the presumptive pancreatic damage associated with OPC poisoning. But there are no large prospective studies incorporating imaging of pancreas to address this.

Respiratory Depression

The most troublesome complication of OP poisoning was respiratory depression which could be due to reasons such as: aspiration of gastric contents, excessive secretions, pneumonia and septicemia complicating adult respiratory distress syndrome. Of the 62 patients, respiratory depression was observed in 23 (37.1%) cases.

Eddleston et al Srilanka (2006) reported that 24% of patients required ventilation. Early recognition of respiratory failure, prompt endotracheal intubations and mechanical ventilation are life saving in severe OP poisoning.

Serum Amylase levels in OP poisoning OP insecticides increase the intraductal pressure and exocrine pancreatic flow. The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could

be due to direct cholinergic hyper stimulation of pancreatic acinar and ductal cells.

In the study, the Amylase levels were significantly elevated at the time of admission [154.61 U/L] and have shown a gradual remission with proper treatment. 51.6% of our patients were found to have hyperamylasemia. There was significant correlation of hyperamylasemia with three of the severe manifestations of OPC poisoning, secretions, fasciculations and bradycardia In our study, there was no significant correlation between elevated Amylase levels and the outcome (mortality).

Lee et al[59] found 36% of OPC poisoning patients to have hyper amylasemia. They also reported significant correlation between elevated amylase levels and clinical severity and development of shock. Singh et al reported hyperamylasemia incidence of 46.95%.But, there was no significant correlation between elevated Amylase levels and the outcome. It is quite possible that part of this amylase is salivary, as demonstrated by Lee *et al* due to increased salivation.

Serum cholinesterase levels in OP poisoning

In studies similar to ours, the relationship between acetylcholinesterase level and the severity of OP poisoning has been examined, but there has been no common conclusion. Goswamy et al[56] have stated that measurement of the acetylcholinesterase level is useful in predicting the prognosis in OP poisoning, but the dominant view is that there is no relationship. In a study

conducted by Aygun et al[60] on patients with OP poisoning, acetylcholinesterase levels on admission were evaluated, and low levels of serum acetylcholinesterase were reported to support the diagnosis of acute OP poisoning, but acetylcholinesterase levels were not related to clinical severity. In the study conducted by Cherian et al on 21 patients with OP poisoning, no significant difference was found in serum acetylcholinesterase levels between the group treated with Pralidoxime and the group that received placebo. Cander et al[61] Turkey reported serum acetylcholinesterase level did not correlate statistically with mortality and length of stay. Some authors suggest that the reduction of serum acetylcholinesterase level and the corresponding clinical manifestation should be evaluated together, which would further benefit treatment planning.

By observing our study, we found that there is significant decrease in serum cholinesterase level in patients with miosis, respiratory failure, bradycardia and fasciculations (severe OPC poisoning).There is no correlation between the cholinesterase levels and the disease outcome from our study.

The results of prospective observational study done at Dept. of chest medicine, King Edward memorial hospital, Mumbai supports our observation that clinical features of miosis, unconsciousness and fasciculations and low cholinesterase levels are strong predictors of the severity of poisoning& ultimately the requirement for ventilator support.

CONCLUSION

Though there have been several studies on OPC poisoning reported in India and worldwide, consensus is yet to be reached on the roles of serum amylase and acetyl cholinesterase in OPC poisoning. Conflicting conclusions and widespread variations have been reported by these studies.

From our observation, it can be suggested that estimation of serum ChE and serum amylase levels would be extremely useful to assess disease severity and helps to identify those at risk of developing the complications of Organophosphorus poisoning.

From the observations of our study, the mean Amylase level in first 24 hours of OP poisoning was 154 U/L which is significantly higher than the control groups.

The bad bedside prognostic factors which correlated very well with serum Amylase levels include secretions, CNS depression, Fasciculations and Respiratory failure .

Similarly the clinical factors related to severity that correlated with acetylcholinesterase include respiratory failure, fasciculations, miosis and bradycardia.

Though there is no significant correlation between the estimation of acetylcholinesterase and amylase with the disease outcome, it is ideal that both these investigations be performed and serially monitored in all cases of OPC poisoning. Considering that most of our patients present late and are bound to

have severe poisoning, it is especially prudent in resource limited setting like ours that both these investigations be done. Based on these levels the atropine dose could be optimized, since a need for higher dose of atropine in severe cases has been evidenced. Thus they may be helpful for the treating physician in careful monitoring and aggressive management of severe cases, thus reducing mortality and saving crucial lives.

However, as the study was limited to a small population due to financial and laboratory constraints, analysis of a larger group would definitely give an insight into the further finer relationship between serum amylase level and clinical severity and outcome in OP poisoning.

A study on serum amylase levels in acute organophosphorus poisoning

PROFORMA

Name : IP No:

Age / Sex: D.O.A:

Residence : urban / rural D.O.D:

Occupation:

Income :

Time between poisoning & admission:

Suicidal / accidental / homicidal reason:

Treatment prior to admission: yes / no

Poison particulars:

Name of poison -

Chemical name:

Trade name :

Quantity consumed :

Nature of poison :

Liquid / powder / granules

Mode of consumption :

Immediate steps taken :

Symptoms:

GIT: vomiting /abdominal cramps / abdominal pain / distension / diarrhoea

CNS: Altered sensorium / Seizures / Blurring of vision / Fasciculations (twitching) paralysis (weakness) / Breathlessness

Others : Salivation / Frothing / Sweating / Lacrimation

Past history:

Similar attempts before : Yes / No

Previous psychiatric illness: Yes / No

Comorbid illness:

Cardiac disease / Chronic lung disease / Renal failure / Gall stone disease neuromuscular disease

H/o drug intake

H/o jaundice

H/o recent surgery

H/o alcohol intake

Clinical profile at the time of admission:

Consciousness	Pulse rate :
Pupil size	BP :
Jaundice	Respiratory rate :

Cyanosis

Fasciculations

Convulsions

RS : Secretions / Respiratory insufficiency

Abdomen : distension / tenderness / palpable mass / bowel sounds + / --

Investigations :

TC- DC- Hb %- ESR-

Blood sugar: Urea : Creatinine :

Liver function tests:

Serum Bilirubin – total: Direct: Indirect:

SGOT: SGPT: ALP: Protein-Total: Albumin: Globulin:

Serum amylase I: II:

Serum cholinesterase I: II:

Complications:

Respiratory failure Hypotension Hypokalemia Pancreatitis

Arrythmias Hepatocellular jaundice

Duration of hospitalization:

Final outcome: Full recovery/ Death

ABBREVIATIONS

2-PAM	-	Pralidoxime
ABG	-	Arterial Blood Gas
Ach	-	Acetyl choline
AChE	-	Acetylcholinesterase
BChE	-	Butyrylcholinesterase
BUN	-	Blood Urea Nitrogen
ChE	-	Cholinesterase
CNS	-	Central Nervous System
ECG	-	Electrocardiogram
GIT	-	Gastrointestinal tract
IMS	-	Intermediate syndrome
NTE	-	Neuropathy Target Esterase
OP	-	Organo Phosphorus
OPC	-	Organo Phosphorus Compounds
OPIDP	-	Organophosphate-Induced Delayed Polyneuropathy
PVC	-	Premature Ventricular Contraction
RBC	-	Red Blood Cell
TEPP	-	Tetraethylpyrophosphate

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CLINICAL FEATURES

S.NO	AGE	SEX	TYPE OF EXPOSURE	REASON FOR ATTEMPTING SUICIDE	URBAN/RURAL	AGENT	PIN POINT PUPIL	SENSORIUM	SECRETIONS	HEART RATE	BP	FASICULATIONS	CONVULSIONS	RESPIRATORY FAILURE	SERUM AMYLASE-I	SERUM AMYLASE-II	SERUM CHOLINESTERASE-I	SERUM CHOLINESTERASE-II	TOTAL COUNT	BLOOD SUGAR	UREA	CREATININE	OUTCOME
1	47	M	I	FA	R	DIM	+	-	++	B	N	+	-	-	230	200	1830	2340	15300	198	32	1.1	A
2	30	F	I	FA	R	DIM	+	-	+	N	N	-	-	-	108	96	7400	6320	8300	148	28	1	A
3	27	M	I	FA	U	PH	+	+	+++	B	H	+	+	+	452	387	940	1650	21800	85	21	0.8	A
4	15	F	I	FA	R	MP	-	-	-	N	N	-	-	-	92	80	6300	6130	7800	92	18	0.8	A
5	45	M	I	FI	R	DIM	-	-	-	N	N	-	-	-	82	78	5940	6700	6400	113	24	1	A
6	32	F	I	FA	R	MC	+	+	++	B	H	+	-	+	312	278	3300	4500	9700	154	15	0.6	A
7	24	M	I	FA	U	PH	-	-	-	N	N	-	-	-	134	114	7800	6730	8700	79	24	0.9	A
8	35	M	I	FA	R	C	-	-	-	N	N	-	-	-	64	68	2300	1750	5400	102	30	0.7	A
9	56	M	I	FI	R	PH	+	-	-	N	N	-	-	-	75	70	5620	4950	6800	125	22	0.7	A
10	25	M	I	O	U	DIM	+	-	+	N	N	+	-	-	48	60	2210	1850	4900	88	19	0.8	A
11	17	F	I	FA	R	MP	+	-	++	B	N	+	-	+	61	71	5630	1740	5600	138	23	0.9	A
12	29	M	I	FA	U	MC	+	+	++	B	H	+	+	+	578	420	660	1370	21300	202	35	1.1	D
13	23	M	I	O	R	Q	+	-	++	B	N	-	-	-	105	85	3200	4820	6700	140	17	0.7	A
14	21	M	I	FA	R	MP	-	-	-	N	N	-	-	-	48	60	5800	6450	7300	98	34	0.8	A
15	33	M	I	FA	U	MC	+	-	++	N	N	+	-	+	364	268	1350	1960	14500	164	32	0.9	A
16	45	M	I	FA	R	Q	-	-	-	N	N	-	-	-	83	80	4960	5700	9200	138	29	0.8	A
17	23	F	I	FA	U	Q	-	-	-	N	N	-	-	-	43	40	5600	6340	5700	89	28	1	A
18	38	M	I	FA	R	DIM	-	-	+	B	N	-	-	-	68	68	2670	3300	10200	112	18	0.9	D
19	35	F	I	FA	R	MC	-	-	++	N	N	-	-	-	48	60	4430	4760	8300	128	28	1.1	A
20	55	M	I	FA	R	MC	+	+	++	B	N	+	+	+	282	240	1370	1850	10800	158	38	0.9	A
21	21	M	I	FA	U	C	+	-	-	N	N	+	-	-	248	210	2650	780	7700	147	29	0.8	A
22	34	M	I	FI	R	Q	+	+	-	B	N	+	-	+	310	268	540	1530	12100	138	18	0.9	A
23	28	M	I	FA	R	PH	+	-	-	N	N	-	-	-	56	50	670	980	5800	98	26	0.8	D
24	37	F	I	FA	R	DIM	-	-	-	N	N	-	-	-	82	80	4750	5320	4300	132	20	1	A
25	48	M	I	FI	R	Q	+	+	++	B	N	+	-	-	278	210	2450	1800	9800	172	32	1.2	A

26	18	F	I	O	R	DIM	+	-	++	N	N	-	-	-	164	110	1240	1830	6800	88	34	0.9	A
27	45	M	I	FA	R	DIM	+	-	+	N	N	+	-	-	72	60	4760	3350	5700	72	26	0.8	A
28	28	F	I	FA	U	MC	+	-	+	B	N	+	-	+	180	168	5630	1750	12300	162	34	1.2	D
29	24	M	I	FA	R	MP	+	+	+++	B	H	+	+	+	210	198	2200	3970	10200	148	26	0.8	A
30	36	M	I	FI	R	MP	+	-	+	N	N	-	-	-	52	60	1730	3340	6300	96	29	0.9	A
31	20	M	I	FA	R	PH	-	+	++	N	N	-	-	-	221	200	6340	4780	9900	88	24	0.8	A
32	34	M	I	FI	R	MC	-	-	-	N	N	-	-	-	37	60	2300	2850	5500	79	27	0.7	A
33	26	M	I	FA	U	MC	+	-	+	B	N	-	-	+	158	110	1640	2760	10200	138	20	0.9	A
34	38	M	I	FA	R	DIM	+	-	++	N	N	+	-	+	179	120	3450	2370	8800	127	27	0.8	A
35	21	F	I	FA	R	C	-	-	-	N	N	-	-	-	38	50	4570	5600	5600	134	45	0.9	A
36	29	F	I	FI	R	DIM	-	-	+	N	N	+	-	-	214	186	1720	2450	7300	96	48	1.4	A
37	17	M	I	FA	U	P	+	-	+	B	N	+	-	+	48	40	3560	2980	4900	112	36	1	A
38	28	F	I	FA	R	PH	+	-	++	B	N	+	-	-	256	210	4780	1750	11200	168	47	1.5	A
39	33	M	E	--	R	C	+	-	+	N	N	+	-	+	29	30	6750	5870	7700	82	17	0.1	A
40	38	M	I	FA	R	Q	+	-	++	N	N	+	-	+	318	260	680	1340	10800	172	32	0.9	D
41	45	M	I	FA	R	DIM	-	-	-	N	N	-	-	-	32	40	780	1650	3800	132	28	0.8	A
42	21	F	I	FA	U	DIM	+	-	+	N	N	+	-	-	168	110	3980	2780	6700	112	19	0.7	A
43	17	F	I	FA	R	MC	-	-	+	N	N	-	-	-	47	40	5830	5400	4600	98	18	0.7	A
44	28	M	I	FI	R	MC	+	-	-	N	N	+	-	-	62	60	4750	3900	5200	89	23	0.9	A
45	31	M	I	FA	R	P	-	-	-	N	N	-	-	-	75	70	4960	6300	6300	78	21	1.2	A
46	24	F	I	FA	U	MP	-	-	+	N	N	-	-	-	58	54	5700	5340	5800	138	19	1.1	A
47	29	M	I	FI	U	DIM	+	+	++	B	N	+	-	+	176	110	3780	2750	9900	127	31	1.2	A
48	36	M	I	O	R	CH	+	-	++	B	H	+	+	+	268	220	1840	940	12100	189	36	1.2	D
49	16	M	I	FA	R	DIM	+	-	+	B	N	-	-	+	247	200	1370	990	10700	132	30	1.1	A
50	23	M	I	FA	R	DIM	+	+	+	N	N	-	-	+	59	60	4780	5300	7800	113	28	0.9	D
51	29	F	I	FA	R	PH	+	-	+	B	N	+	-	+	340	290	2730	1100	11800	178	30	1.1	A
52	56	M	I	FI	R	MC	-	-	++	N	N	+	-	-	38	40	1840	2700	5700	99	28	0.9	A
53	37	F	I	FI	R	MP	+	-	+	N	N	+	-	-	57	40	1640	3670	4400	89	27	1.1	D
54	29	M	I	FA	U	PH	+	-	+	N	N	-	-	-	72	87	3300	3560	6500	84	19	0.8	A
55	32	M	I	FA	R	DIM	+	+	+	B	N	+	-	+	430	290	750	1100	13200	221	31	1.2	A
56	21	F	I	FA	R	Q	+	+	++	N	N	+	-	+	196	119	2560	1340	9700	148	36	1.2	A
57	64	F	I	FI	U	CH	+	-	+	N	N	+	-	+	168	140	2300	1780	8300	137	32	1.1	A
58	18	M	I	O	R	P	-	-	+	N	N	+	-	+	278	240	1680	2350	10700	162	29	1	A
59	43	M	I	FA	R	MC	-	-	+	N	N	-	-	-	48	50	4980	5320	6300	192	18	0.8	A
60	38	M	I	FA	R	Q	+	-	+	N	N	-	-	-	118	89	3640	3430	5600	88	19	0.9	A

61	29	F	I	FI	U	DIM	-	-	+	N	N	+	-	-	164	110	2370	1830	7700	108	23	0.8	A
62	58	M	I	FI	R	Q	+	-	+	N	N	+	-	-	58	53	5300	4750	6800	94	18	0.8	A
63	22	F	-	-	R	-	-	-	-	N	N	-	-	-	53	25	4750	4900	9200	113	31	0.8	A
64	43	M	-	-	R	-	-	-	-	N	N	-	-	-	14	65	5300	4930	5700	126	36	0.9	A
65	19	F	-	-	R	-	-	-	-	N	N	-	-	-	15	89	7840	7650	10200	79	30	0.8	A
66	45	M	-	-	R	-	-	-	-	N	N	-	-	-	43	44	7900	7690	8300	102	28	1	A
67	25	M	-	-	R	-	-	-	-	N	N	-	-	-	21	52	6300	5900	10800	125	30	0.9	A
68	34	F	-	-	R	-	-	-	-	N	N	-	-	-	37	27	3780	4800	7700	88	28	1.1	A
69	26	F	-	-	U	-	-	-	-	N	N	-	-	-	89	42	4300	4700	12100	138	27	0.9	A
70	19	M	-	-	R	-	-	-	-	N	N	-	-	-	78		5750	5300	5800	202	19	0.8	A
71	49	M	-	-	R	-	-	-	-	N	N	-	-	-	53	34	4750	3600	4300	140	31	0.9	A
72	44	M	-	-	R	-	-	-	-	N	N	-	-	-	88	47	4900	5300	5500	98	36	0.8	A
73	27	F	-	-	R	-	-	-	-	N	N	-	-	-	11	28	6700	7120	10200	164	32	1	A
74	23	M	-	-	R	-	-	-	-	N	N	-	-	-	19	30	5300	4930	8800	138	29	1.2	A
75	17	M	-	-	R	-	-	-	-	N	N	-	-	-	25	14	6300	5740	5600	89	18	0.9	A
76	58	M	-	-	U	-	-	-	-	N	N	-	-	-	56	15	5740	6320	7300	112	19	0.8	A
77	22	M	-	-	R	-	-	-	-	N	N	-	-	-	32	43	7300	4980	4900	128	27	1.2	A
78	25	F	-	-	R	-	-	-	-	N	N	-	-	-	41	21	6750	4760	11200	158	20	0.8	A
79	54	F	-	-	R	-	-	-	-	N	N	-	-	-	25	37	4200	3870	7700	147	27	0.9	A
80	24	M	-	-	R	-	-	-	-	N	N	-	-	-	42	89	4860	4430	10800	132	45	1.4	A
81	56	F	-	-	U	-	-	-	-	N	N	-	-	-	53	78	6750	6300	3800	112	48	1	A
82	42	M	-	-	R	-	-	-	-	N	N	-	-	-	14	53	5800	5340	6700	98	36	1.5	A
83	32	M	-	-	R	-	-	-	-	N	N	-	-	-	15	24	5750	6340	4600	89	47	0.1	A
84	42	M	-	-	R	-	-	-	-	N	N	-	-	-	43	39	5400	5740	5200	78	33	0.9	A
85	28	F	-	-	U	-	-	-	-	N	N	-	-	-	21	30	4750	4400	6300	138	32	0.8	A
86	29	F	-	-	R	-	-	-	-	N	N	-	-	-	37	33	5460	4700	5800	127	52	0.7	A
87	16	M	-	-	R	-	-	-	-	N	N	-	-	-	89	93	3800	4350	10700	189	18	0.7	A
88	33	M	-	-	R	-	-	-	-	N	N	-	-	-	78	80	1980	3670	7800	132	32	0.9	A
89	37	M	-	-	R	-	-	-	-	N	N	-	-	-	53	40	7560	5400	11800	113	28	1.2	A
90	21	F	-	-	R	-	-	-	-	N	N	-	-	-	78	69	5300	5640	5700	111	21	1.1	A
91	64	F	-	-	R	-	-	-	-	N	N	-	-	-	25	25	7800	6700	4400	89	18	1.2	A
92	33	M	-	-	U	-	-	-	-	N	N	-	-	-	65	33	5360	4980	6500	84	24	1.2	A
93	45	F	-	-	R	-	-	-	-	N	N	-	-	-	89	79	4750	5300	13200	129	15	1.1	A
94	18	M	-	-	R	-	-	-	-	N	N	-	-	-	44	43	5340	4780	9700	148	24	0.9	A
95	22	M	-	-	U	-	-	-	-	N	N	-	-	-	52	21	4670	3900	8300	137	30	1.1	A

96	28	M	-	-	R	-	-	-	-	N	N	-	-	-	27	37	5100	5800	7300	162	22	0.9	A
97	31	F	-	-	R	-	-	-	-	N	N	-	-	-	42	31	4930	5640	4900	112	19	1.1	A
98	37	F	-	-	R	-	-	-	-	N	N	-	-	-	52	44	3480	4450	11200	88	23	0.8	A
99	40	M	-	-	R	-	-	-	-	N	N	-	-	-	34	53	6700	5780	7700	108	35	1.2	A
100	24	M	-	-	R	-	-	-	-	N	N	-	-	-	47	32	5800	3780	10800	89	17	1.2	A
101	20	F	-	-	R	-	-	-	-	N	N	-	-	-	28	40	3900	5640	3800	130	34	0.7	A
102	33	M	-	-	U	-	-	-	-	N	N	-	-	-	30	27	4870	4300	6700	99	32	0.9	A

Key to master Chart

I - Ingestion
Fa - Family Problems
Fi - Financial Problems
O - Others (Chronic illness, love failure, etc.,)
W - Water
A - Alive
D - Death
R - Rural
U - Urban
N - Normal
B - Bradycardia
H - Hypotension
Q - Quinolphos
PH - Phorate
P - Parathion
MP - Methyl Parathion
MC - Monochrotophos
DiM - Dimethoate
CH - Chlorpyrifos
C - Cyclopyrifos